

Accepted Manuscript

Accepted Manuscript (Uncorrected Proof)

Title: The Influence of Diabetes on Outcomes of Patients with Sepsis

Authors: Laura Menezes Silveira¹, Simone Costa Silva¹, Mariele Lenhari¹, Thaissa Pinto de Melo¹, Antônio Ruffino-Netto², Angelita Maria Stabile^{1,*}

1. *University of São Paulo at Ribeirão Preto College of Nursing, Ribeirão Preto, Brazil.*
2. *Department of Social Medicine, Hospital of the Ribeirão Preto Medical School, Ribeirão Preto, Brazil.*

To appear in: ***Journal of Client-centered Nursing Care***

Received date: 2025/02/19

Revised date: 2025/08/09

Accepted date: 2025/08/17

This is a “Just Accepted” manuscript, which has been examined by the peer-review process and has been accepted for publication. A “Just Accepted” manuscript is published online shortly after its acceptance, which is prior to technical editing and formatting and author proofing. Journal of Client-centered Nursing Care provides “Just Accepted” as an optional and free service which allows authors to make their results available to the research community as soon as possible after acceptance. After a manuscript has been technically edited and formatted, it will be removed from the “Just Accepted” Web site and published as a published article. Please note that technical editing may introduce minor changes to the manuscript text and/or graphics which may affect the content, and all legal disclaimers that apply to the journal pertain.

Please cite this article as:

Menezes Silveira, L., Costa Silva, S., Lenhari, M., Pinto de Melo, T., Ruffino-Netto, A. & Stabile, A. M., 2026. The Influence of Diabetes on Outcomes of Patients with Sepsis. To be published in *Journal of Client-centered Nursing Care* [Preprint].

Doi: <http://dx.doi.org/10.32598/JCCNC.12.1.961.1>

Accepted Manuscript (Uncorrected Proof)

Abstract

Background: Sepsis is characterized by a set of physiological reactions that occur in an unregulated manner in response to an infection. Type 2 diabetes mellitus (T2DM) is a common comorbidity of patients with sepsis. This study aimed to compare the clinical outcomes and nursing workload of patients with sepsis with and without T2DM, as well as to describe their admission characteristics, clinical progression, and blood glucose levels.

Methods: This retrospective cohort study reviewed medical records of adult intensive care patients at a high-complexity, public, tertiary hospital in São Paulo, Brazil. From 2015-2019, two groups of 102 patients (with and without T2DM) were consecutively included. Data collected encompassed sociodemographic, clinical admission data (including prognostic scores like Sequential Organ Failure Assessment [SOFA], Simplified Acute Physiology Score III [SAPS III], and Acute Physiology and Chronic Health Evaluation II [APACHE II]), ICU progression, patients' outcomes (e.g., ICU discharge or death), blood glucose levels, and glycemic variability (GV). Nursing workload was assessed by the Nursing Activity Score (NAS). Statistical analysis used SPSS (v.25) using Student t-test or Mann-Whitney test for numerical variables, and Pearson's Chi-square test or Fisher's exact test for categorical variables. The level of statistical significance adopted was $p < 0.05$.

Results: T2DM patients showed higher mortality ($p=0.012$), elevated prognostic scores (APACHE II $p=0.035$, SAPS III $p=0.033$), and greater glycemic variability ($p<0.001$ for all related metrics) compared to non-T2DM patients. While NAS was similar between groups ($p=0.644$), it was associated with death in both ($p=0.000$ and $p=0.007$, respectively).

Conclusion: T2DM significantly influences both ICU and hospital outcomes, leading to higher mortality rates in sepsis patients. The T2DM group presented with more severe admission conditions (indicated by higher APACHE II, SAPS III, and a greater number of comorbidities) and exhibited higher average blood glucose and greater glycemic variability. While overall NAS was similar, a higher NAS was consistently associated with mortality, highlighting heightened care demands for critically ill patients who progress to death.

Keywords: Diabetes mellitus, Sepsis, Blood glucose, Mortality, Critical care

Highlights

- Sepsis is a severe condition characterized by unregulated physiological responses to infection. T2DM is a common comorbidity in septic patients, associated with increased susceptibility to infections.
- The prognostic scores, APACHE II and SAPS III, were higher in the T2DM group than in the non-T2DM group. Furthermore, the scores upon admission showed a worse prognosis for patients with T2DM.
- A higher glycemic variability and a higher occurrence of deaths were observed in the group of patients with T2DM.
- The Nursing Activity Score was associated with death in groups with and without Diabetes Mellitus

Plain Language Summary

Sepsis is a severe body reaction to infection, while many of these patients also have type 2 diabetes (T2DM). Our study examined the impact of T2DM on clinical outcomes and nursing workload in patients with sepsis. We compared patients with sepsis and T2DM to those without T2DM in an ICU by analyzing medical records. We found that patients with T2DM had a higher mortality rate and were more severe upon admission. They also experienced more infections and greater blood sugar variability. Interestingly, nursing workload and ICU length of stay were similar between the groups; however, patients who died required more nursing care. This study reinforces that T2DM negatively influences sepsis outcomes, highlighting the need for more specialized care.

Introduction

Type 2 diabetes mellitus (T2DM) is the most common clinical class of diabetes mellitus (DM), present in 90%–95% of cases, usually diagnosed after the age of 40, and associated with population aging, obesity, and physical inactivity. T2DM occurs due to a decrease in pancreatic beta-cell function, resulting in disorders of insulin action and secretion, which lead to impaired metabolic responses to insulin. Global statistics show that approximately 537 million people live with DM, and by 2045, the prevalence of DM is expected to be 783 million, and 85% of these people will be living in low- and middle-income countries (*International Diabetes Federation, 2021*).

The association between DM and infection is well known clinically and is related to several causal pathways, including impaired immune responses in the hyperglycemic environment and altered lipid metabolism. People with DM are nearly twice as likely to be hospitalized and die from infection-related causes than those without DM (Carey et al., 2018). These infections may progress to a condition of greater clinical severity and a higher risk of death, such as sepsis, a condition associated with a higher frequency of hypoglycemia, hyperglycemia, and glycemic variability (GV) in patients with DM (Hirsch, 2015). Approximately 20% of patients with sepsis also have T2DM (Silveira et al., 2017). Moreover, the combination of DM and sepsis has been associated with worse clinical outcomes and increased infectious complications and mortality (Frydrych et al., 2017).

Sepsis is the body's reaction to infection, during which various unregulated physiological responses that lead to organ dysfunction occur (Singer et al., 2016). The clinical severity of sepsis is associated with high morbidity and mortality, while the costs associated with hospitalization and the complications and organ dysfunctions of sepsis make it a priority public health problem (Reinhart et al., 2017).

A previous study reported that a higher GV and percentage of deaths were observed among patients with DM and sepsis or septic shock than among patients without DM. In this study, patients

with DM had a higher need for blood glucose examinations and interventions for regularization, which could imply an increased demand for care provided by the nursing staff (Silveira et al., 2017).

Nurses directly care for patients with sepsis. When the patient is continuously infused with insulin, more frequent glycemic examinations are required, consequently increasing the workload of the nursing team (Huang et al., 2024). Thus, whether patients with T2DM and sepsis require more time of care from the nursing team should be investigated, since the increased nursing team workload is associated with an increased risk of death in the intensive care units (ICUs) (Lee et al., 2017).

Considering that sepsis and T2DM are complex problems affecting the health of the population, the estimated increasing number of people with DM in the coming years, and the greater susceptibility of these individuals to infections, differences in metabolic behaviors that may influence the course and outcome of sepsis should be determined. Therefore, this study aimed to compare the clinical outcomes and nursing team workload of patients with sepsis with and without T2DM, as well as to describe their admission characteristics, clinical progression, and blood glucose levels.

Materials and methods

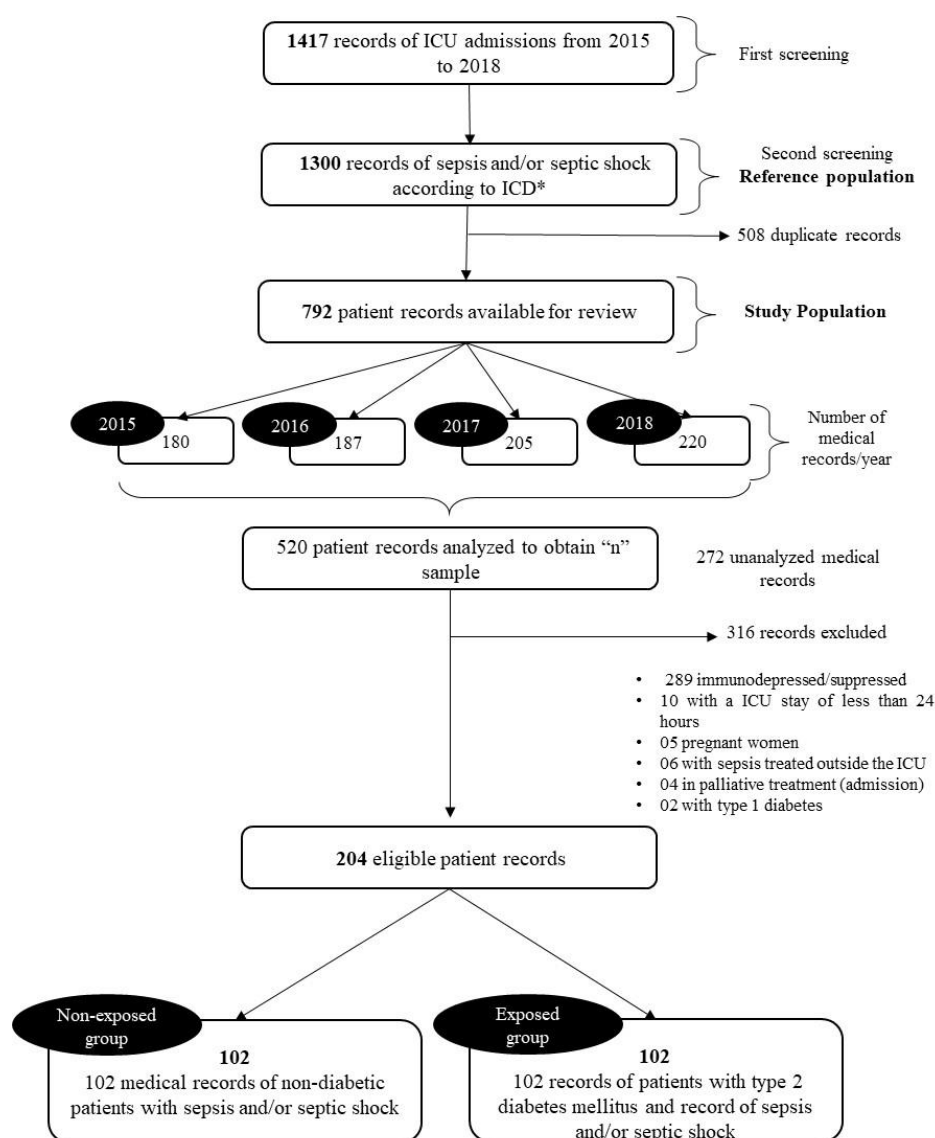
Design, setting, and sample

This was a retrospective cohort study. The exposed group was patients with sepsis and T2DM and the non-exposed group was patients with sepsis and no T2DM, both admitted to the ICU. The study was conducted in a public tertiary hospital that offers highly complex care, located in the countryside of the state of São Paulo, Brazil. The institution consists of 815 general beds and 105 ICU beds, with 14 ICU beds specified for the care of adult clinical, and surgical patients.

For both groups, the following candidates were considered eligible: persons aged ≥ 18 years, of either sex, with a minimum stay of 24 hours in the ICU from January 2015 to December 2018. Pregnant women, and immunodepressed patients (transplanted, presenting malignant neoplastic

and/or hematological diseases, and people living with HIV/AIDS), with other types of DM and patients indicated for palliative treatment at the time of ICU admission were excluded.

Medical records were intentionally (non-probabilistically) selected, and the number of patients included in the sample was calculated based on the estimated mortality in the exposed group, i.e., patients with sepsis and T2DM ($P_1 = 90\%$), and in the non-exposed group, i.e., patients with sepsis without T2DM ($P_2 = 70\%$), considering $\alpha = 5\%$ and $\beta = 10\%$, respectively, according to the following formula: $n = \frac{(Z\alpha + Z\beta)^2 \times (P_1Q_1 + P_2Q_2)}{(P_1 - P_2)^2}$. The calculation resulted in 78.8 patients. To explore other variables, a sample of 102 patients was used for each group (Figure 1).



* International Classification of Diseases

Figure 1 - Detailing of the screening, selection, and inclusion process of the analyzed medical records.

Data collection

Data were extracted from physical and electronic medical records and registered in a semi structured form containing the following variables: sociodemographic data (date of birth, sex, skin color), clinical data upon admission (i.e., up to 24 h after the ICU admission, including the presence of comorbidities such as systemic arterial hypertension, heart disease, dyslipidemia, chronic

obstructive pulmonary disease, and chronic kidney disease), body mass index [BMI], organ dysfunction scores/prognosis as Sequential Organ Failure Assessment [SOFA], Simplified Acute Physiology Score [SAPS III], and Acute Physiology and Chronic Health Evaluation II [APACHE II]), clinical outcomes (days of ICU stay, date and type of ICU outcome (discharge or death), date and type of hospital outcome [discharge or death], positive culture records, surgical treatment, number of clinical complications, and septic shock), and glycemic data (glycemic records obtained at bedside using a glucometer during the entire ICU stay and the average body glucose levels on admission calculated based on blood glucose values). For the calculation of the Nursing Activity Score (NAS), information was directly collected from the electronic medical record, utilizing data from all ICU admission records (in hours).

Assessment scores and tools

The **SOFA** score evaluates the severity of organ dysfunction in critically ill patients using six parameters: respiratory, renal, hepatic, cardiovascular, neurological, and coagulation function. Each system receives a score ranging from 0 (normal) to 4 (most altered), resulting in a final score between 0 and 24. The calculation considers the worst value observed for each parameter within the first 24 hours after ICU admission (Vincent et al., 1996). The parameters assessed include the ratio of the partial pressure of oxygen in arterial blood (PaO_2) to the fraction of inspired oxygen (FiO_2) ($\text{PaO}_2/\text{FiO}_2$ ratio) (respiratory), creatinine (renal), total bilirubin (hepatic), mean arterial pressure, and use/dose of vasoactive drugs (cardiovascular), platelet count (coagulation), and Glasgow coma scale (GCS) (neurological). Each domain with a score equal to or greater than two indicates organ dysfunction, with the total number of dysfunctions determined by the number of domains meeting this criterion upon admission. Additionally, the SOFA score is used to monitor clinical progression and estimate prognosis, as higher scores are associated with greater morbidity

and mortality. The validity and reliability of this tool in assessing morbidity in critical illness, especially in the context of sepsis and its progression, have been confirmed (Arts et al., 2005).

The **SAPS III** score is used to assess disease severity and estimate the mortality risk of patients within the first hours of ICU admission. It considers variables such as age, prior hospitalization and/or hospital sector, presence of comorbidities, oncology treatments, solid tumors, hematologic cancer, heart failure, cirrhosis, use of vasoactive drugs before ICU admission, type of ICU admission (urgent or scheduled), reason for ICU admission (cardiovascular, hepatic, digestive, neurological, or surgical), and, in the case of surgical reasons, the type of surgery (transplantation, trauma, polytrauma, cardiac surgery, neurosurgery, or other). Additional factors include nosocomial infections, respiratory infections, GCS, systemic blood pressure, heart rate, body temperature, PaO_2 , $\text{PaO}_2/\text{FiO}_2$ ratio, total bilirubin, creatinine, leukocytes, platelets, and hydrogen potential of hydrogen (pH). For each variable, points are assigned based on predefined physiological ranges and clinical conditions, contributing to a total score that typically ranges from 0 to 217. The calculation is based on data obtained in the first hour of ICU admission (SAKR et al., 2008). A higher SAPS III score indicates greater disease severity and a correspondingly increased predicted probability of mortality. Moreover, the SAPS III score demonstrates a strong discriminative ability, proving effective in differentiating between patients who are likely to survive and those who will progress to death (Ledoux et al., 2008).

The **APACHE II** score estimates the patient's prognosis and is calculated based on three main components (Knaus et al., 1985). First, an Acute Physiology Score (APS) is derived from the worst values of twelve physiological parameters recorded within the first 24 hours of ICU admission, where points are assigned (typically from 0 to 4 for each parameter) based on the degree of deviation from predefined normal ranges. Second, an age-adjusted score is added, with increasing points for older age categories. Third, a chronic health score accounts for pre-existing severe organ insufficiency

or immunocompromised status. These three component scores are then summed to yield a total APACHE II score, which typically ranges from 0 to 71. Higher scores indicate a greater physiological derangement and a higher predicted risk of mortality. The specific variables contributing to the APS include: temperature, mean arterial pressure (MAP), respiratory and heart rates, PaO₂/FiO₂ ratio, arterial pH, sodium levels, potassium levels, creatinine, hematocrit, leukocytes, and GCS. In addition to these, age and the presence of chronic diseases are integrated into the total score. APACHE II is a widely validated and robust severity-of-disease classification system, recognized for its good discriminative power and predictive accuracy in estimating mortality for critically ill patients (Ali et al., 2025).

The **NAS** is divided into seven major categories and includes a total of 23 items, with weight values ranging from a minimum of 1.2 to a maximum of 32.0. The total score represents the percentage of nursing time spent per shift in direct patient care, with a maximum achievable percentage of 176.8%. Each percentage point corresponds to 14.4 minutes of nursing care provided by the nursing team (Miranda et al., 2003; Queijo & Padilha, 2009). It is derived from an instrument translated and validated for use in Brazil (Queijo & Padilha, 2009). This validation study, conducted across 13 Brazilian ICU, confirmed the instrument's robust psychometric properties. Specifically, its internal consistency, an important measure of reliability, was demonstrated by Cronbach's alpha values ranging from 0.79 to 0.82 for its seven categories. Moreover, construct validity was established through factorial analysis, revealing a factor structure consistent with that of the original version. These findings collectively support the NAS as a reliable and valid tool for assessing nursing team workload in the intensive care setting.

The **GV** was calculated using the glycemic amplitude, that is, by subtracting the lowest from the highest blood glucose value. For the standard deviation (SD), the mean of all blood glucose values obtained in each group was calculated, and the differences were squared. Then, the mean of

these squared differences was calculated, and finally, the square root was extracted. The coefficient of variation (CV%) was calculated by applying the following formula: $CV\% = [\text{standard deviation of blood glucose} / \text{mean blood glucose}] \times 100$.

Data analysis

The collected data were double-entered into a spreadsheet and, after validation, were imported into the Statistical Package for Social Sciences software version 25 (IBM, 2017). Based on descriptive statistics of absolute frequency and relative frequencies, measures of central tendency and variability were performed. To analyze the differences between numerical variables, the Student's t-test or Mann-Whitney test was used (when non-normal distribution was indicated by the Shapiro-Wilk test). For categorical variables, relationships were denoted through the application of the Pearson's chi-square test. Statistical significance was considered as $p < 0.05$.

This manuscript was prepared following the recommendations of the Strengthening the Reporting of Observational studies in Epidemiology guidelines (STROBE).

Results

The sample consisted of 204 patients, 102 for each group. In both groups, the majority were male, white, and older than 60 years (Table 1). The presence of T2DM was associated with the ICU death as an outcome in patients with sepsis ($p = 0.012$). A similar result was observed in relation to the hospital outcome, in which the number of deaths in the group of patients with T2DM was higher when compared to that in the group without T2DM ($p = 0.033$) (Table 1).

Table 1 - Description of sociodemographic variables and outcomes according to sepsis groups: patients with and without T2DM.

	Patients with T2DM	Patients without T2DM	p value*
Sex	N (%)	N (%)	
Female	50 (49.0)	39 (38.2)	0.120
Male	52 (51.0)	63 (61.8)	
Color			
White	76 (74.5)	88 (86.3)	0.034
Non-white	26 (25.5)	14 (13.7)	
Age			
< 60 years	40 (39.2)	32 (31.4)	0.241
≥ 60 years	62 (60.8)	70 (68.6)	
ICU outcome			
Discharge	43 (42.2)	61 (59.8)	0.012
Death	59 (57.8)	41 (40.2)	
Hospital outcome			
Discharge	22 (50.0)	43 (70.5)	0.033
Death	21 (48.8)	18 (29.5)	

*Pearson's chi-square test

The characteristics upon admission and clinical evolution are described in Table 2. The main causes of ICU admission in the T2DM group were septic shock (n = 32; 31.5%), sepsis (n = 20; 19.9%), and pneumonia (n = 7; 7.0%). In the non-T2DM group, they were septic shock (n = 28; 27.5%), sepsis (n = 27; 26.5%), and postoperative complications of neurological surgery (n = 8; 7.8%).

Table 2 - Description of admission variables and clinical evolution in the ICU according to sepsis groups: patients with and without T2DM during sepsis.

	Patients with T2DM	Patients without T2DM	<i>p</i> value
Admission variables			
Number of comorbidities	Mean (Med $\pm$ SD) 4.9 (5.0 $\pm$ 0.1)	Mean (Med $\pm$ SD) 2.66 (2.5 $\pm$ 0.1)	<0.001 [#]
BMI	29.4 (28.7 $\pm$ 0.8)	26.9 (24.9 $\pm$ 0.7)	0.017 [#]
Number of organic dysfunctions	2.9 (3.0 $\pm$ 0.1)	3.0 (3.0 $\pm$ 0.1)	0.858 [#]
Prognostic scores			
SOFA	9.6 (10.0 $\pm$ 0.3)	9.6 (9.0 $\pm$ 0.4)	0.904 ^{##}
APACHE II	30.2 (30.0 $\pm$ 0.7)	28.0 (28.0 $\pm$ 0.7)	0.035 ^{##}
SAPS III	77.4 (79.5 $\pm$ 1.5)	71.8 (70.0 $\pm$ 2.0)	0.033 ^{##}
Evolution variables			
Sepsis record	N (%)	N (%)	
Yes	57 (55.9)	70 (68.6)	0.060*
No/no record	45 (44.1)	32 (31.4)	
Septic shock record			
Yes	89 (87.3)	84 (82.4)	0.329*
No/no record	13 (12.7)	18 (17.6)	
Surgical treatment			
Yes	54 (52.9)	53 (52.0)	0.889*
No	48 (47.1)	49 (48.0)	
Positive culture(s)			
Yes	85 (85.0)	69 (71.9)	0.025*
No	15 (15.0)	27 (28.1)	
Number of ICU complications	Mean (Med $\pm$ SD) 2.5 (2.0 $\pm$ 0.1)	Mean (Med $\pm$ SD) 2.2 (2.0 $\pm$ 0.1)	0.095 [#]
Hospitalization time			
Days of hospitalization prior to ICU	13.1 (6.5 $\pm$ 1.7)	13.0 (6.0 $\pm$ 1.7)	0.611 [#]
Days of ICU stay	13.4 (11.0 $\pm$ 1.0)	12.7 (11.0 $\pm$ 1.0)	0.402 [#]
Days of hospital stay	42.8 (27.0 $\pm$ 4.8)	47.1 (30.5 $\pm$ 5.2)	0.476 [#]

Med - median, SD - standard deviation, *Pearson's chi-square test, #Mann-Whitney, ## Student's t-test

In the group with T2DM, the main sites of infection were the bloodstream in 54 (52.9%) patients, the urinary tract in 39 (38.2%), and the respiratory tract in 37 (36.3%). In the group of

patients without T2DM, the sites were the bloodstream in 49 (48.0%) patients, the urinary tract in 40 (39.2%), and the respiratory tract in 29 (28.4%). The main microorganisms identified in the T2DM group were *Acinetobacter baumannii* in 34 (33.3%) patients, followed by fungi in 24 (21.5%), and *Klebsiella pneumoniae* in 21 (20.6%) patients. In the non-diabetic group were: *Acinetobacter baumannii* in 38 (27.2%), *Klebsiella pneumoniae* in 21 (20.6%), *Escherichia coli* in 18 (17.6%), and *Staphylococcus aureus* in 16 (15.7%) patients.

Eighty-two complications registered in the medical records were found, and in both groups, pressure injury was a common complication in the group with T2DM (n = 44; 43.1%) and without T2DM (n = 32; 31.4%), as well as acute kidney injury requiring dialysis therapy (n = 30 [29.4%] and n = 29 [28.4%] in the group with and without T2DM, respectively).

The mean blood glucose upon admission and throughout hospitalization ($p = 0.000$) and the GV (in the methods used for this assessment) ($p = 0.000$) were higher in patients with T2DM, compared to non-diabetic ones (Table 3).

Table 3 - Description and analysis related to glycemic profile according to sepsis groups: patients with and without T2DM during sepsis.

	Patients with T2DM	Patients without T2DM	p value [#]
Blood glucose	Mean (Med $\pm$ SD)	Mean (Med $\pm$ SD)	
Mean blood glucose at admission	204 (185.9 $\pm$ 10.7)	143.2 (142.0 $\pm$ 6.3)	<0.001
Mean blood glucose during hospitalization	185.6 (185.9 $\pm$ 5.2)	135.4 (131.1 $\pm$ 3.3)	<0.001
Glycemic variability			
Amplitude (mmol/L)	227.9 (219.0 $\pm$ 12.8)	122.5 (101.5 $\pm$ 7.8)	<0.001
SD (mmol/L)*	51.8 (45.6 $\pm$ 2.7)	26.9 (22.6 $\pm$ 1.5)	<0.001
CV%	27.2 (24.6 $\pm$ 1.2)	19.5 (18.5 $\pm$ 0.9)	<0.001
Glycemic measurements			
Blood glucose $\leq$ 3.8 mmol/L	0.5 (0.0 $\pm$ 0.0)	0.4 (0.0 $\pm$ 0.0)	<0.001
Blood glucose 3.8 to < 6.1 mmol/L	3.2 (2.0 $\pm$ 0.5)	6.0 (4.0 $\pm$ 0.7)	<0.001
Blood glucose 6.1 to < 7.7 mmol/L	4.6 (2.0 $\pm$ 0.6)	7.3 (3.5 $\pm$ 0.8)	<0.001
Blood glucose 7.7 to < 9.9 mmol/L	6.7 (3.0 $\pm$ 0.9)	5.3 (3.0 $\pm$ 0.6)	<0.001
Blood glucose $\geq$ 9.9 mmol/L	12.8 (6.0 $\pm$ 1.9)	4.5 (1.0 $\pm$ 0.8)	<0.001

Med - median, SD - standard deviation, *Millimoles per liter #Mann-Whitney

The NAS did not differ between T2DM and non-diabetic patients ($p = 0.644$); however, the NAS score was associated with mortality in both the T2DM group and the non-diabetic group ($p = 0.000$ and $p = 0.007$, respectively) (Table 4).

Table 4 - Nursing care metrics and patient outcomes in sepsis, stratified by TDM2 Status.

Caremetrics	Patients with T2DM			Patients without T2DM		
	Discharge	Death	<i>P</i> value	Discharge	Death	<i>P</i> value
	Mean (Med $\pm$ SD)	Mean (Med $\pm$ SD)		Mean (Med $\pm$ SD)	Mean (Med $\pm$ SD)	
NAS	86.7 (86.0 $\pm$ 1.0)	91.0 (91.7 $\pm$ 1.0)	0.000 ^t	86.5 (87.0 $\pm$ 0.9)	92.0 (91.0 $\pm$ 1.2)	0.007 ^t

Med – median, SD – standard deviation, ^t t Student.

Discussion

Evidence from this study showed that the number of deaths, number of comorbidities, severity/prognosis on admission (APACHE II and SAPS III), and glycemic indices were higher in patients with T2DM compared to those without T2DM.

For Tiwari et al. (2011), T2DM worsens the prognosis and increases the morbidity and mortality in infection. However, few specific studies have been conducted to understand the clinical evolution in patients with sepsis and T2DM, including variables expressing the complexity of the clinical picture of sepsis. The meta-analysis (Wang et al., 2017) results about sepsis and DM suggested that DM does not affect the outcomes of patients with sepsis. However, in this review (Wang et al., 2017), the authors included ten articles in the analysis, and of these, only five specified the type of DM as type 2, thus hindering the generalization of conclusions.

No statistically significant age-related differences were found in the groups of patients with and without T2DM; however, the number of comorbidities and BMI were higher in the group of patients with T2DM. Our findings are in line with other studies that have examined the presence of

overweight and comorbidities in patients with T2DM. A study of 1104 patients with sepsis, of whom 241 (21.8%) were persons with DM, patients with T2DM were older and had a higher BMI (Van Vught et al., 2016). Additionally, patients with T2DM had a high prevalence of comorbidities. A study by Li et al. (2021) observed that while the number of comorbidities increased with age, a high prevalence was already present across nearly all age groups (e.g., 80% in those aged 18–39 and 91% in those aged 40–59). This suggests that T2DM is generally associated with a substantial burden of chronic conditions, irrespective of age. These findings highlight the significant impact of T2DM on the overall health of patients, reinforcing its pervasive association with comorbidities and increased BMI across all age groups.

Obesity is one of the main factors related to the T2DM development. Patients with obesity and patients with DM are more susceptible to infections and are more likely to develop complications from infections (Yang et al., 2020). Although obesity is considered a risk factor for sepsis, a multicenter study showed that those who were obese received lower doses of antimicrobial agents, lower fluid volumes, and had lower hospital mortality (Arabi et al., 2013). Another study showed that morbid obesity was a protective factor against death from sepsis (Kuperman et al., 2013).

In contrast, studies have shown that obesity can aggravate the septic status by increasing the oxidative stress, which can cause brain (Vieira et al., 2015), lung, and liver damage (Petronilho et al., 2016), leading to worse outcomes (Papadimitriou-Olivgeris et al., 2016). Thus, whether obesity in patients with DM would be a protective factor during sepsis and/or if there is any inherent mechanism in patients with DM and obesity capable of modifying the prognosis of sepsis should be clarified.

It was observed that the group with T2DM had more records of positive microbiological culture when compared to the group without T2DM. Other studies also showed a similar finding, that is, high rates of infection in the DM group (Carey et al., 2018).

A. baumannii is a prevalent pathogen in hospitals, easily adapting to the environment, commonly resistant to available antimicrobials, and associated with increased morbidity and mortality (Ballouz et al., 2017). Infection with this organism is associated with prolonged use of broad-spectrum antibiotics, prolonged hospitalization, patient severity (Gulen et al., 2015), sepsis development (Freire et al., 2016), and inappropriate antimicrobial therapy in patients with sepsis (Shorr et al., 2014).

In the group with T2DM, fungi were the second microorganisms most frequently recorded in cultures. Although other risk factors are associated with fungal infection in critically ill patients, according to Singh et al. (2016), DM may be an independent risk factor for fungal infection in critically ill patients, and the chance of these patients acquiring a fungal infection is twice as high as in patients without T2DM.

Studies infer that the occurrence of respiratory, skin, soft tissue, urinary tract, genital, and perineal infections in people with DM is associated with inadequate glycemic control (Hine et al., 2017). Thus, glycemic control in the context of DM and infections should be considered as a practice valuable by the multidisciplinary team, both for the prevention of infections that can trigger sepsis, and in monitoring patients with sepsis who may acquire new infections.

Most frequently reported complications in both groups were pressure injury and acute kidney injury. Hemodynamic instability (mean arterial pressure, ≤ 65 mmHg) indicates insufficient peripheral circulation and tissue perfusion (Engels et al., 2016). People with DM are more susceptible to wound development (Cox & Roche, 2015) due to vascular (macroangiopathy and microangiopathy) and metabolic (hyperglycemia and hyperinsulinemia) changes (Zambonato et al., 2013).

In relation to acute kidney injury, sepsis is one of the main risk factors for its development. Patients with DM often have other health problems in addition to DM, such as dyslipidemia, obesity, and cardiovascular disease. These problems increase the chance of acute kidney injury in critical

conditions (Poston & Koyner, 2019). A French case-control study demonstrated that DM is not associated with acute kidney injury in patients with sepsis or septic shock; however, it represents an independent risk factor for persistent renal dysfunction in patients with acute kidney injury in the ICU who, even after discharge, show creatinine levels above normal parameters (Venot et al., 2015).

Regarding the glycemic variables, mean, amplitude, SD, and CV% of blood glucose values were higher in the group with T2DM than those without T2DM. Previous studies present similar findings (Silveira et al., 2017; Krinsley et al., 2013). Blood glucose instability in patients with DM requires more attention from the healthcare team because blood glucose fluctuations play a significant role in vascular endothelial dysfunction, onset of cardiovascular events (Torimoto et al., 2013), increased oxidative stress, and modification of the kidney structure and function, with consequently increased creatinine levels (Ying et al., 2016). Moreover, GV is correlated with increased length of hospital stay (Mendez et al., 2013).

Currently, the American Association of Clinical Endocrinologists and the American Diabetes Association propose glycemic targets between 7.7 and 9.9 mmol/L for critically ill patients, regardless of whether or not DM is present, avoiding blood glucose levels of <5.5 mmol/L (Sociedade Brasileira de Diabetes, 2015). The guideline of the Surviving Sepsis Campaign recommends maintaining the blood glucose levels between 7.8 and 9.9 mmol/L (Evans et al., 2021).

Regarding the GV measurements, in this study, the mean CV% was 29.8% in patients with T2DM and 22.4% in those without T2DM. Every 10% increase in CV% of blood glucose levels is estimated to increase the risk of death by 1.2 times in critically ill patients. The CV% of glycemia has been associated with mortality, regardless of age, disease severity, DM, and hypoglycemia (Lanspa et al., 2013). In critically ill patients without DM, the risk of death is higher than in those with DM (odds ratio, 1.3 vs. 1.1), respectively (Lanspa et al., 2013). The SD was also higher in patients with T2DM. Blood glucose SD values of >2.7 mmol/L indicate high GV, i.e., higher blood glucose

instability. The Brazilian Society of Diabetes (Sociedade Brasileira de Diabetes, 2019) recommends that SD be <2.8 mmol/L or at most $1/3$ of the blood glucose mean.

Previous studies have shown that patients with DM tolerate a wider range of blood glucose levels than patients without DM (Sechterberger et al., 2013). From this perspective, DM is seen as a protective factor against the risk of death in critically ill patients (Krinsley et al., 2013). However, the evidence from this study shows a higher GV and a higher occurrence of deaths in patients with T2DM. Blood glucose care is important for all patients with sepsis, regardless of whether or not they have T2DM. The health team should be aware of the glycemic levels of patients with sepsis and constantly reevaluate the control procedures.

Other authors infer that hyperglycemia (blood glucose level >11.1 mmol/L) in the situation of ICU admission is a common event in patients with sepsis associated with increased mortality up to 30 days post-admission, regardless of the presence of T2DM (Van Vught, 2017). One study showed that during sepsis, hyperglycemia, hypoglycemia, and GV are independent risk factors for death during hospitalization (Chao et al., 2017). Moreover, the high occurrence of deaths in the group of patients with DM may be associated with the immunological characteristics of T2DM, such as increased C-reactive protein, Tumor Necrosis Factor α (TNF- α), and interleukins IL-6 and IL-8, causing abnormalities in response to infections (Koh et al., 2012).

Regarding the workload and time demand of the nursing staff, the study results showed no differences in these two variables in the comparison between groups. However, the mean NAS in this study was 89.1% for patients with and 88.6% for those without T2DM, which represents about 21 h of care, characterizing a high work demand for professionals. The average workload was found to be higher than that presented in other ICU studies, where NAS averages ranged from 70% to 79% (Nassiff et al., 2018; Padilha et al., 2015), which may have implications for the number of professionals involved in care. Furthermore, NAS was associated with death in groups with and

without T2DM. The association between the NAS and mortality has been the subject of ICU studies, indicating that the mean NAS is higher in patients who progress to death compared to those who survive. Higher NAS values reflect greater clinical complexity and severity, as more critically ill patients, including those with sepsis, require increased monitoring, therapeutic interventions, and invasive support, thereby raising the demands on the nursing team. This increased nursing workload correlates with negative outcomes, including a higher risk of death (Ross et al., 2025). Another study reinforces that, although the mean NAS during the first 24 hours is elevated in ICUs with many cases of sepsis, the hypothesis that a high workload serves as an independent predictor of mortality may vary according to the clinical severity measured by other scores (e.g., APACHE II). Nevertheless, high NAS values are generally associated with greater risk and complexity, which are common in sepsis cases (Nassif et al., 2018).

Some limitations associated with this study should be mentioned, particularly the retrospective model and the data collected from medical records, where the data quality is not controlled; therefore, the study is subject to information bias. However, studies designed specifically for outcome analysis in patients with and without T2DM are few. Thus, with the present study, it is expected to contribute to the expansion of knowledge regarding the particularities of patients with T2DM and sepsis.

Conclusion

In conclusion, patients with T2DM and sepsis had worse ICU and hospital outcomes, presented more severe conditions, had a higher number of infections, and had a higher GV during sepsis. The workload and length of nursing care are similar in the group of patients with sepsis. Evidence from this study is expected to further clarify the role of T2DM in the clinical course of patients with sepsis. As the health team increases its knowledge, it can propose improvements by qualifying the care offered.

Ethical Considerations

Compliance with ethical guidelines

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of under no. 5.776.917 September 29, 2022, with the need for written informed consent waived, as we used secondary data.

Acknowledgement: This work was carried out with the support of the Coordination for the Improvement of Higher Education Personnel - Brazil (CAPES) - Financing Code 001 (CAPES is a Brazilian governmental agency that organizes and regulates graduate programs in Brazil, but it is not a research funding agency). The authors acknowledge the National Council for Scientific and Technological Development (CNPq) for the scholarship granted to the main researcher.

Authors' contributions: Menezes Silveira L: Contributed to the conception and design, acquisition of data, analysis and interpretation of data, and drafting the article. Costa Silva S, and Lenhari Gonçalves M: Contributed to the acquisition of data, and critical review of the intellectual content. Pinto de Melo T: Contributed to drafting the article, and critical review of the intellectual content. Ruffino-Netto A: Contributed to the conception and design, and reviewed it critically for important intellectual content. Stabile AM: Contributed to the conception and design, analysis and interpretation of data, and drafting the article. All authors read and approved the final manuscript.

Funding: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of interests: The author(s) declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

References

- Ali, A.H.D., et al., 2025. Discriminatory Performance of APACHE II Score and the Prediction of Mortality within the ICU in Patients with Sepsis Admitted to the ICU. *Materia Socio-Medica*, 37(2), pp. 153-158. [DOI:<http://10.5455/msm.2025.37.153-158>]
- Arabi, Y. M., et al., & Cooperative Antimicrobial Therapy of Septic Shock (CATSS) Database Research Group, 2013. Clinical characteristics, sepsis interventions and outcomes in the obese patients with septic shock: an international multicenter cohort study. *Critical Care*, 17(2), pp. R72. [DOI:<https://10.1186/cc12680>]
- Arts, D.G., et al., 2005. Reliability and accuracy of Sequential Organ Failure Assessment (SOFA) scoring. *Critical Care Medicine*, 33(9), pp. 1988-1993. [DOI:<https://10.1097/01.ccm.0000178178.02574.ab>]
- Ballouz, T., et al., 2017. Risk factors, clinical presentation, and outcome of *Acinetobacter baumannii* bacteremia. *Frontiers in Cellular and Infection Microbiology*, 4(7), pp.156. [DOI:<https://10.3389/fcimb.2017.00156>]
- Carey, I. M., et al., 2018. Risk of infection in type 1 and type 2 diabetes compared with the general population: A matched cohort study. *Diabetes Care*, 41(3), pp. 513–521. [DOI:<https://10.2337/dc17-2131>]
- Chao, H. Y., et al., 2017. Association of in-hospital mortality and dysglycemia in septic patients. *PLoS One*, 12(1), pp. e0170408. [DOI:<https://10.1371/journal.pone.0170408>]
- Cox, J., & Roche, S., 2015. Vasopressors and development of pressure ulcers in adult critical care patients. *American Journal of Critical Care*, 24(6), pp. 501–510. [DOI:<https://doi.org/10.4037/ajcc2015123>]
- Engels, D., et al., 2016. Pressure ulcers: Factors contributing to their development in the OR. *AORN Journal*, 103(3), pp. 271–281. [DOI:<https://10.1016/j.aorn.2016.01.008>]
- Evans, L., et al., 2021. Surviving sepsis campaign: International Guidelines for management of sepsis and septic shock 2021. *Intensive Care Medicine*, 47(1)1, pp. 1181–1247. [DOI:<https://10.1007/s00134-021-06506-y>]
- Freire, M. P., et al., 2016. Bloodstream infection caused by extensively drug-resistant *Acinetobacter baumannii* in cancer patients: high mortality associated with delayed treatment rather than with the degree of neutropenia. *Clinical Microbiology and Infectious Diseases*, 22(4), pp. 352–358. [DOI:<https://10.1016/j.cmi.2015.12.010>]

Frydrych, L. M., et al., 2017. Diabetes and sepsis: risk, recurrence, and ruination. *Frontiers in Endocrinology*, 30(8), pp. 271. [DOI:<https://10.3389/fendo.2017.00271>]

Gulen, T. A., et al., 2015. Clinical importance and cost of bacteremia caused by nosocomial multidrug-resistant *Acinetobacter baumannii*. *International Journal of Infectious Diseases*, 38, pp. 32–35. [DOI:<https://10.1016/j.ijid.2015.06.014>]

Hine, J. L., et al., 2017. Association between glycaemic control and common infections in people with Type 2 diabetes: a cohort study. *Diabetic Medicine*, 34(4), pp. 551–557. [DOI:<https://0.1111/dme.13205>]

Hirsch, I. B., 2015. Glycemic variability and diabetes complications: Does it matter? Of course it does! *Diabetes Care*, 38(8), pp. 1610–1614. [DOI:<https://10.2337/dc14-2898>]

Huang, M., et al., 2024. Insulin Infusion Protocols for Blood Glucose Management in Critically Ill Patients: A Scoping Review. *Critical Care Nurse*, 44(1), pp. 21-32. [DOI:10.4037/ccn2024427]

International Diabetes Federation. (2021). IDF Diabetes Atlas (10th ed.). Brussels, Belgium, Viewed 17 February 2025, <https://diabetesatlas.org/atlas/tenth-edition>.

Knaus, W. A., et al., 1985. APACHE II: a severity of disease classification system. *Critical Care Medicine*, 13(10), 818–829.

Koh, G. C., et al., 2012. The impact of diabetes on the pathogenesis of sepsis. *European Journal of Clinical Microbiology & Infectious Diseases*, 31(4), pp. 379–388. [DOI:<https://10.1007/s10096-011-1337-4>]

Krinsley, J. S., et al., 2013. Diabetic status and the relation of the three domains of glycemic control to mortality in critically ill patients: an international multicenter cohort study. *Critical Care*, 17(2), pp. R37. [DOI:<https://10.1186/cc12547>]

Kuperman, E. F., et al., 2013. The impact of obesity on sepsis mortality: A retrospective review. *BMC Infectious Diseases*, 16(13), pp. 377. [DOI:<https://10.1186/1471-2334-13-377>]

Lanspa, M. J., et al., 2013. Moderate glucose control is associated with increased mortality compared with tight glucose control in critically ill patients without diabetes. *Chest*, 143(5), pp. 1226–1234. [DOI:<https://10.1378/chest.12-2072>]

Ledoux D., Canivet J-L., E Preiser J-Ch., Damas P, 2008. SAPS 3 admission score: An external validation in a general intensive care population. *Intensive Care Medicine*, 34(10):1873-7. [DOI: 10.1007/s00134-008-1187-4]

- Lee, A., et al., 2017. Are high nurse workload/staffing ratios associated with decreased survival in critically ill patients? A cohort study. *Annals of Intensive Care*, 7(46), pp. 46. [DOI:<https://10.1186/s13613-017-0269-2>]
- Li, X., et al., 2021. Prevalence of comorbidities and their associated factors in patients with type 2 diabetes at a tertiary care department in Ningbo, China: a cross-sectional study. *BMJ Open*, 11(1), pp. e040532. [DOI:<https://10.1136/bmjopen-2020-040532>]
- Mendez, C. E., et al., 2013. Increased glycemic variability is independently associated with length of stay and mortality in noncritically ill hospitalized patients. *Diabetes Care*, 36(12), pp. 4091-4097. [DOI:<https://10.2337/dc12-2430>]
- Miranda, D. R., et al., 2003. Nursing activities score. *Crit Care Medicine*, 31(2), pp. 374–382. [DOI:<https://10.1097/01.CCM.0000045567.78801.CC>]
- Nassiff, A., et al., 2018. Nursing workload and patient mortality at an intensive care unit. *Texto & Contexto - Enfermagem*, 27(4), pp. e0390017. [DOI:<https://10.1590/0104-07072018000390017>]
- Padilha, K. G., et al., 2015. Nursing activities score: An updated guideline for its application in the intensive care unit. *Revista da Escola de Enfermagem da USP*, 49, pp. 131–137. [DOI:<https://10.1590/S0080-623420150000700019>]
- Papadimitriou-Olivgeris, M., et al., 2016. The role of obesity in sepsis outcome among critically ill patients: A Retrospective Cohort Analysis. *BioMed Research International*, 2016, pp. 5941279. [DOI:<https://10.1155/2016/5941279>]
- Petronilho, F., et al., 2016. Obesity exacerbates sepsis-induced oxidative damage in organs. *Inflammation*, 39(6), pp. 2062–2071. [DOI:<https://10.1007/s10753-016-0444-x>]
- Poston, J. T., Koyner J.L., 2019. Sepsis associated acute kidney injury. *BMJ*, 9(364), pp. k4891. [DOI:<https://10.1136/bmj.k4891>]
- Queijo, A. F., Padilha, K. G., 2009, Nursing Activities Score (NAS): Cross-cultural adaptation and validation to Portuguese language. *Revista da Escola de Enfermagem da USP*, 43, pp. 1018–1025. [DOI:<https://10.1590/S0080-62342009000500004>]
- Reinhart, K., et al., 2017. Recognizing sepsis as a global health priority — A WHO resolution. *New England Journal of Medicine*, 377(5), pp. 414–417. [DOI:<https://10.1056/NEJMp1707170>]
- Ross, P., et al., 2023. Nursing workload and patient-focused outcomes in intensive care: A systematic review. *Nursing Health Science*, 25(4): pp. 497-515. [DOI:<https://10.1111/nhs.13052>]

Sechterberger, M. K., et al., 2013. The effect of diabetes mellitus on the association between measures of glycaemic control and ICU mortality: a retrospective cohort study. *Critical Care*, 17(2), pp. R52. [DOI:<https://10.1186/cc12572>]

Shorr, A. F., et al., 2014. Predictors of hospital mortality among septic ICU patients with *Acinetobacter* spp. bacteremia: A cohort study. *BMC Infectious Diseases*, 14, pp. 572. [DOI:<https://10.1186/s12879-014-0572-6>]

Silveira, L. M., et al., 2017. Glycaemic variability in patients with severe sepsis or septic shock admitted to an intensive care unit. *Intensive and Critical Care Nursing*, 41, pp. 98–103. [DOI:<https://10.1016/j.iccn.2017.01.004>]

Singer, M., et al., 2016. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*, 315(8), pp. 801–810. [DOI:<https://10.1001/jama.2016.02871>]

Singh, G., et al., 2016. Risk factors for early invasive fungal disease in critically ill patients. *Indian Journal of Critical Care Medicine*, 20(11), pp. 633–639. [DOI:<https://10.4103/0972-5229.194007>]

Sociedade Brasileira de Diabetes, 2015, Posicionamento oficial SBD nº 03/2015: Controle da glicemia no paciente hospitalizado (32 p.). São Paulo, Brazil. Viewed 17 February 2025, <https://www.diabetes.org.br/publico/images/2015/pdf/posicionamentos-acesso-livre/posicionamento-3.pdf>

Sociedade Brasileira de Diabetes, 2019, Diretrizes da Sociedade Brasileira de Diabetes 2019-2020, São Paulo, Brazil: Clannad. Viewed 17 February 2025, <http://www.saude.ba.gov.br/wp-content/uploads/2020/02/Diretrizes-Sociedade-Brasileira-de-Diabetes-2019-2020.pdf>

Tiwari, S., et al., 2011. Sepsis in diabetes: A bad duo. *Diabetes & Metabolic Syndrome*, 5(4), pp. 222–227. [DOI:<https://10.1016/j.dsx.2012.02.026>]

Torimoto, K., et al., 2013. Relationship between fluctuations in glucose levels measured by continuous glucose monitoring and vascular endothelial dysfunction in type 2 diabetes mellitus. *Cardiovascular Diabetology*, 2(12), pp. 1. [DOI:<https://10.1186/1475-2840-12-1>]

Van Vught, L. A., et al., 2017. Diabetes is not associated with increased 90-day mortality risk in critically ill patients with sepsis. *Critical Care Medicine*, 45(10), pp. e1026–e1035. [DOI:<https://10.1097/ccm.0000000000002590>]

Van Vught, L. A., et al., 2016. Association of diabetes and diabetes treatment with the host response in critically ill sepsis patients. *Critical Care*, 20(1), pp. 252. [DOI:<https://10.1186/s13054-016-1429-8>]

Venot, M., et al., 2015. Acute kidney injury in severe sepsis and septic shock in patients with and without diabetes mellitus: A multicenter study. *PloS One*, 10(5), pp. e0127411. [DOI:[https://10.1371/journal.pone.0127411](https://doi.org/10.1371/journal.pone.0127411)]

Vincent, J. L. et al., 1996. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis – Related Problems of the European Society of Intensive Care Medicine. *Intensive and Care Medicine*, 22(7), pp. 707-710. [DOI:[https://10.1007/bf01709751](https://doi.org/10.1007/bf01709751)]

Vieira, A. A., et al., 2015. Obesity promotes oxidative stress and exacerbates sepsis-induced brain damage. *Current Neurovascular Research*, 12(2), pp. 147–154. [DOI:[https://10.2174/1567202612666150311111913](https://doi.org/10.2174/1567202612666150311111913)]

Wang, Z., et al., 2017. Association between diabetes mellitus and outcomes of patients with sepsis: A meta-analysis. *Medical Science Monitor*, 23, pp. 3546–3555. [DOI:[https://10.12659/msm.903144](https://doi.org/10.12659/msm.903144)]

Yang, W. S., et al., 2020. The association between body mass index and the risk of hospitalization and mortality due to infection: A prospective cohort study. *Open Forum Infectious Diseases*, 8(1): pp. ofaa545. [DOI:[https://10.1093/ofid/ofaa545](https://doi.org/10.1093/ofid/ofaa545)]

Ying, C., et al., 2016. Blood glucose fluctuation accelerates renal injury involved to inhibit the AKT signaling pathway in diabetic rats. *Endocrine*, 53(1), pp. 81–96. [DOI:[https://10.1007/s12020-016-0867-z](https://doi.org/10.1007/s12020-016-0867-z)]

Zambonato, B. P., et al., 2013. Association of Braden subscales with the risk of development of pressure ulcers. *Revista Gaúcha de Enfermagem*, 34(1), pp. 21–28. [DOI:[https://10.1590/s1983-14472013000200003](https://doi.org/10.1590/s1983-14472013000200003)]